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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/924,654	08/07/2001	Richard D. Goold	PC-0049 CIP	7397
27904	7590	01/21/2004	EXAMINER	
INCYTE CORPORATION 3160 PORTER DRIVE PALO ALTO, CA 94304			NICKOL, GARY B	
			ART UNIT	PAPER NUMBER

1642

DATE MAILED: 01/21/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/924,654

Applicant(s)

GOOLD ET AL.

Examiner

Gary B. Nickol Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 08 December 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-15 is/are pending in the application.
- 4a) Of the above claim(s) 5-15 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-4 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

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Response to Amendment

Re: Gould *et al.*

Earliest date of priority: March 15, 1996 (SEQ ID NO:4)

The Amendment filed December 8, 2003 in response to the Office Action mailed September 3, 2003 is acknowledged and has been entered.

Claims 1-15 are pending.

Claims 5-15 have been withdrawn from further consideration by the examiner under 37 CFR 1.142(b) as being drawn to non-elected inventions.

Claims 1-4 are currently under consideration.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Rejection Maintained:

Claims 1-4 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement wherein the claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention for the reasons of record in the Office Action mailed September 3, 2003, pages 3-7.

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Initially, applicant's appear to argue (page 5) that since the claimed invention has utility the skilled artisan would clearly know how the use the claimed invention in toxicology testing, drug discovery, and in the detection and diagnosis of various cancers. This argument has been considered but is not found pertinent, as the previously mailed Action (09/03/2003) did not raise any issues under utility. Further, as applicants correctly note, the Examiner withdrew the rejection under 35 USC 101 made in the first office action (mailed 03/17/2003). This rejection was made because there were specific questions as to the interpretation of the data in the disclosure. Subsequently, applicant's response (Applicant's response of 06/16/2003; page 5) was deemed persuasive to withdraw the rejection under utility. Hence, in this particular case, the issues underlying utility were deemed separable with regards to the issues governing enablement of the claimed invention under 35 USC 12, 1st paragraph.

The primary arguments made with regards to the invention are whether one of ordinary skill in the art would know how to predictably use the claimed polypeptide based solely on the analysis of mRNA expression. Applicants argue (page 6) that they disagree with the Examiner's allegation that mRNA expression does not correlate with nor predict polypeptide expression. Applicants refer to exhibit A (Lewin, B.) to illustrate that for most genes a major control point probably exists at the level of transcription during the interaction of RNA polymerase with its promoter. In contrast, Applicants argue that the references cited in the previous action represent comparatively unusual mechanisms of gene regulation downstream of transcription. Extrapolating from Lewin, applicants argue that the question is not whether there is the potential for post-transcriptional regulation of SEQ ID NO:4 expression but whether one skilled in the art would have a reasonable expectation that SEQ ID NO:4 correlates with the levels of SEQ ID

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NO:3. These arguments have been carefully considered but are not found persuasive. Even if gene regulation occurred predominately at the level of transcription initiation, such an observation does not provide evidence to refute the unpredictability of equating mRNA production with the corresponding polypeptide, because, as applicants noted (page 7), there are many steps in the pathway leading from DNA to protein, and *all* of them can in principle be regulated. Further, the allegation that post-transcriptional regulation, in comparison to regulation at the initiation of transcription, is an unusual event (i.e. rare event) may be attributed to less research in the area of post-transcriptional regulation. Jansen *et al.* (Pediatric Res., Vol. 37, No. 6, 1995 pages 681-686) teach that regulation of mRNA translation, although less well characterized than the regulation of gene transcription, is now recognized as one of the major regulatory steps in the control of gene expression. Thus, while the initiation of gene transcription may represent a highly regulated step, it is also recognized that post-transcriptional events represent major steps in the control of gene expression.

Thus, applicants have not provided a reasonable nexus between 1) the assertion that mRNA levels are usually a good indicator of protein levels with 2) the knowledge that regulation of genes occurs at the level of transcription because there are many steps in the pathway leading from DNA to protein and regulation during the initiation of transcription does not necessitate ruling out gene regulation during later steps. In fact, Lewin acknowledges that control of gene expression can occur at multiple levels, and moreover states that “production of RNA cannot inevitably be equated with production of protein” (Exhibit A, Lewin, 1st page of Chapter 29).

Applicants further disagree (pages 7-8) with the notion that for the claimed protein to serve as a clinically relevant diagnostic marker, it must be present in cancer tissue to the

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exclusion of normal tissue or vice versa. Applicants submit that the Examiner has acknowledged the differential expression of the "polynucleotide" encoding the claimed polypeptide wherein such recognition is sufficient to indicate the presence of cancer and does not require the complete exclusion of the marker in one tissue versus the other. This argument has been considered but is not found persuasive because applicant's arguments are directed solely to the experiments preformed with microarray analysis, an analysis that measures *polynucleotide* expression. As set forth above and previously, the disclosure and arguments of record do not provide sufficient evidence to support the assertion that the mRNA levels are predictive of the *claimed* protein's level in a cell. Thus, applicant's arguments have not been found persuasive and the rejection is maintained.

All other rejections and or objections are withdrawn in view of applicant's amendments and arguments there to.

No claim is allowed.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

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the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary B. Nickol Ph.D. whose telephone number is 703-305-7143. The examiner can normally be reached on M-F, 8:30-5:00 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached at 703-308-6564. After, January 12, the phone number for Y. Eyler will be (571) 272-0871. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Gary B. Nickol, Ph.D.
Examiner
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GBN
January 14, 2004

